

MALLET et al
Appl. No. 10/511,343
Atty. Dkt. 3665-122
RESPONSE
March 11, 2009

REMARKS

Reconsideration is requested.

Claims 35 and 53 have been revised above in response to the Notice of Non-Compliant Amendment. Entry and consideration of the Amendment filed November 26, 2008 with the above additional revisions are requested.

The Notice of Non-Compliant Amendment is submitted to have been mailed in error and with unnecessary delay.

Specifically, the comments of the Notice appear to make clear that the Examiner appreciated the intent of the applicants in deleting the term “suitable”. The Examiner has not indicated any confusion in the Amendment in this regard nor has the Examiner indicated any plausible alternative to the use of double brackets in the amendments of claims 35 and 53. Further, the remarks of the Amendment state as follows:

The objected-to term “suitable” has been further deleted from the rejected claims in response to the Examiner’s comments.

The applicants submit that the Amendment of November 26, 2008 is clear with regard to the deletion of the term “suitable”.

The applicants note in this regard that the MPEP provides for the Patent Office to enter otherwise technically non-conforming amendments where the amendment can be understood in context. Specifically, MPEP § 714 G. provides as follows:

G. Entry of Amendments, Directions for, Defective
The directions for the entry of an amendment may be defective. Examples include inaccuracy in the paragraph number and/or page and line designated, or a lack of precision where the paragraph or section to which insertion of the amendment is directed occurs. If the correct place of

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entry is clear from the context, the amendatory paper will be properly amended in the Technology Center and notation thereof, initialed in ink by the examiner, who will assume full responsibility for the change, will be made on the margin of the amendatory paper. In the next Office action, the applicant should be informed of this alteration in the amendment and the entry of the amendment as thus amended. The applicant will also be informed of the nonentry of an amendment where defective directions and context leave doubt as to the intent of applicant. See http://www.uspto.gov/web/offices/pac/mpep/documents/0700_714.htm#sect714 (March 20, 2008).

The Amendment of November 26, 2008 is clear in the deletion of the term "suitable" and the Amendment should have been entered without requiring further instruction from the applicants.

Moreover, further delay by the Patent Office in issuing the Notice of Non-Compliant Amendment in this regard is submitted to have been inappropriate and contrary to the MPEP. Specifically, the month delay in forwarding the electronically-filed Amendment of November 26, 2008 to the Examiner (PAIR indicates the Amendment was "Forwarded to the Examiner" on December 30, 2008) and the over 2 month delay by the Examiner in mailing the Notice of March 4, 2009 is contrary to MPEP § 714.05 which provides as follows:

Actions by applicant, especially those filed near the end of the period for reply, should be inspected immediately upon filing to determine whether they are completely responsive to the preceding Office action so as to prevent abandonment of the application. If found inadequate, and sufficient time remains, applicant should be notified of the deficiencies and warned to complete the reply within the period. See MPEP § 714.03.

All amended applications forwarded to the examiner should be inspected at once to determine the following:

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(C) If the amendment is fully responsive (MPEP § 714.03 and § 714.04) and complies with 37 CFR 1.121 >(MPEP § 714)<.

The applicants submit that Notice of Non-Compliant Amendment mailed March 4, 2009 was mailed in error and with unnecessary delay.

The Examiner is requested to either withdraw or vacate the Notice of March 4, 2009 or indicate the Examiner's belief that the Notice was properly mailed so that the applicants may consider whether further action by way of a Petition, for example, is appropriate.

Claims 1-34, 37-42, 50 and 54-57, have been canceled, without prejudice.

Claims 68-71 have been added. The claims have been revised, without prejudice.

Support for the amended claims may be found, for example, on page 1, lines 6-10; page 3, lines 3-5, 16-20 and 24-25; the Figures and experimental section of the description, such as pages 25-28. No new matter has been added. These amendments are made without prejudice or disclaimer and solely in order to facilitate reconsideration of this application. In particular, applicant reserves his right to file a continuation and/or divisional application at a later stage, and the present amendment shall not be considered as an admission of the objection or as a waiver of any subject matter.

The objection to claim 58 is obviated by the above amendments. Withdrawal of the objection is requested.

To the extent not obviate by the above amendments, the Section 112, first paragraph "enablement", rejection of claims 35, 36, 43-46, 54-58 an 64-67, is traversed.

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Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The claims are supported by an enabling disclosure.

The objected-to term “suitable” has been further deleted from the rejected claims in response to the Examiner’s comments. Moreover, claim 54 has been canceled, without prejudice. Further, the claims are directed to plasmids and recombinant viral vectors, as described by the specification.

Withdrawal of the Section 112, first paragraph “enablement” rejection is requested.

To the extent not obviated by the above, the following rejections are traversed:

the Section 103 rejection of claims 35, 36 and 46 over Barry (Human Gene Therapy 12:1103-1108; 2001), in view of Paulding (JBC 274:2532-2538);

the Section 103 rejection of claim 43 over Barry and Paulding and Ramezani (Mol. Ther. 2:458-469; 2000);

the Section 103 rejection of claims 40, 44, 64 and 65 over Barry, Paulding, Ramezani and Rogers (JBC 274:6421-6431; 1999);

the Section 103 rejection of claims 41, 42, 45-51, 66 and 67 over Barry, Paulding, Ramezani, Rogers and Aronov (Journal of Molecular Neuroscience, 12:131-145; 1999); and

the Section 103 rejection of claims 52, 56 and 59 over Barry view of Chang (Curr. Gene Ther. 2:237-251; 2001).

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Reconsideration and withdrawal of the Section 103 rejections are requested in view of the above and the following distinguishing comments.

The applicants have previously noted deficiencies in the primary reference and demonstrated a synergistic effect from the claimed invention. The applicants urge the Examiner to appreciate

that an unexpected property of the product (i.e., a synergistic effect) is evidence of its unobviousness. See In re Albrecht, 198 USPQ 208 (CCPA 1978).

The applicants have tested combinations of these posttranscriptional regulatory elements and unexpectedly found that they could cooperate or act in synergy to provide positive effects on transgene expression. This is confirmed by the declaration form Dr Jacques Mallet, inventor, and by the Brun *et al.* reference, of record. The applicants submit that the cited combination of art would not have suggested the vector according to the claimed invention not its effect in enhancing expression of the transgene.

The Examiner is understood to not be persuaded by the Declaration evidence that the Central Polypurine Tract (cPPT) is not a posttranscriptional regulatory element. See the Declaration of Jacques Mallet indexed in the PTO IFW on January 31, 2008. The Examiner is urged to appreciate that the declarant is a specialist in the construction of lentiviral vectors and has provided evidence in the Declaration based on scientific articles published in reviewed journals. As stated on page 2 of the Declaration, the "cPPT sequence" used by Barry *et al.* is the "flap sequence" or "HIV-1 DNA flap nuclear transporter" used by Zennou *et al.*. In addition to the Declaration of record, the applicants believe this distinction is confirmed by Barry *et al.* which states as follows:

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"*The incorporation of a central polypurine tract (cPPT) (Charneau and Clavel, 1991; Follenzi et al., 2000; Zennou et al., 2000)*..." (see left column, lines 8-9, page 1104 of Barry et al.). As also noted in the Declaration, the cPPT sequence increases the vector transduction efficacy by about 10 fold, due to the stimulation of the genome vector nuclear import [see Zennou et al., 2001 (naming in particular Dr. Jacques Mallet as author), 2001, page 448, right column, and Zennou et al., 2000, page 180, Figure 6B].

The comparison and analysis of Dr Jacques Mallet in the evidence of record is thus to be considered by the Examiner as a confirmation of the advantageous additional synergistic effects produced by the vectors according to the present invention which comprise **at least two distinct postranscriptional regulatory elements** functional in mammalian cells, **each comprising a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR.**

It is further to be noted that cPPT, even if considered to be a post transcriptionnal regulatory element, is not a post transcriptionnal regulatory element comprising a UTR region of a eukaryotic mRNA, as claimed.

The applicant further note that the additional synergistic effects on transgene expression are clearly demonstrated in the experimental part of the application as filed wherein the claimed vectors have been tested and specific combinations of postranscriptional regulatory elements have been validated for particular cell types, namely glial cells, fibroblasts and neuronal cells. These methods are described in new claims 68-71.

Withdrawal of the Section 103 rejections is requested.

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The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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